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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/622,377	07/18/2003	Thomas J. Jentsch	59572(46865)	9926

7590 02/27/2007

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EXAMINER	
HAMA, JOANNE	
ART UNIT	PAPER NUMBER
1632	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/622,377	JENTSCH, THOMAS J.	
	Examiner	Art Unit	
	Joanne Hama, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42-67* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant filed a response to the Non-Final Action of May 5, 2006 on October 5, 2006.

Claims 1-41 are cancelled. Claims 42, 48, 50, 53 are amended.

Claims 42-67 are under consideration.

Withdrawn Rejections

35 U.S.C. § 101

Applicant's arguments, see page 7 of Applicant's arguments, filed October 5, 2006, with respect to the rejection of claims 42-67 have been fully considered and are persuasive. Applicant indicates that claims 42, 48, 50, and 53 have been amended to include a limitation that the cells are "in vitro." The rejection of claims 42-53 has been withdrawn.

35 U.S.C. § 112, 1st parag.

Applicant's arguments, see pages 7-21 of Applicant's response, filed October 5, 2006, with respect to the rejection of claims 42-67 have been fully considered. Applicant has indicated that the claims relate to cells or cell preparations and their use. They do not relate to mice. In light of the claim amendments indicating that the claimed cells are "in vitro," the Examiner finds Applicant's arguments persuasive. The rejection of claims 42-67 has been withdrawn.

New/Maintained Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 42-67 are newly rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for

a) an in vitro cell comprising a transgene construct that overexpresses chloride channel ClC-7 and transgene constructs that directly reduce endogenous expression of chloride channels ClC-3 and ClC-6, wherein the cell exhibits higher levels of ClC-7 expression than that of ClC-3 or ClC-6,

b) an in vitro cell comprising a transgene construct that overexpresses chloride channel ClC-7 and transgene constructs that directly reduce endogenous expression of chloride channels ClC-3, ClC-4, ClC-5, and ClC-6, wherein the cell exhibits higher levels of ClC-7 expression than that of ClC-3, ClC-4, ClC-5, and ClC-6,

c) an in vitro cell comprising a transgene construct that overexpresses chloride channel ClC-7 and transgene constructs that directly reduce endogenous expression of chloride channels ClC-1, ClC-2, ClC-Ka, ClC-Kb, ClC-3, ClC-4, ClC-5, and ClC-6, wherein the cell exhibits higher levels of ClC-7 expression than that of ClC-1, ClC-2, ClC-Ka, ClC-Kb, ClC-3, ClC-4, ClC-5, and ClC-6,

d) an in vitro cell comprising a transgene construct that overexpresses chloride channel ClC-3 and a transgene construct that directly reduces endogenous expression of chloride channel ClC-7, wherein the cell exhibits higher levels of ClC-3 and reduced levels of ClC-7,

e) an in vitro cell comprising a transgene construct that overexpresses chloride channel ClC-4 and a transgene construct that directly reduces endogenous expression of chloride channel ClC-7, wherein the cell exhibits higher levels of ClC-4 and reduced levels of ClC-7,

f) an in vitro cell comprising a transgene construct that overexpresses chloride channel ClC-4 and a transgene construct that directly reduces endogenous expression of chloride channels ClC-3, ClC-5, ClC-6, and ClC-7, wherein the cell exhibits higher levels of ClC-4 and reduced levels ClC-3, ClC-5, ClC-6, and ClC-7,

g) an in vitro cell comprising a transgene construct that overexpresses chloride channel ClC-6 and a transgene construct that directly reduces endogenous expression of chloride channel ClC-7, wherein the cell exhibits higher levels of ClC-6 and reduced levels of ClC-7,

h) an in vitro cell comprising transgene constructs that overexpress the chloride channels ClC-3 and ClC-6 and a transgene construct that directly reduces endogenous expression of chloride channel ClC-7, wherein the cell exhibits higher levels of ClC-3 and ClC-6 and reduced levels of ClC-7,

i) an in vitro cell comprising transgene constructs that overexpress chloride channels ClC-1, ClC-2, ClC-Ka, ClC-Kb, ClC-3, ClC-4, ClC-5, and ClC-6

and a transgene construct that directly reduces endogenous expression of ClC-7, wherein the cell exhibits higher levels of ClC-1, ClC-2, ClC-Ka, ClC-Kb, ClC-3, ClC-4, ClC-5, and ClC-6 and reduced levels of ClC-7.

j) an in vitro cell comprising a transgene construct that overexpresses chloride channel ClC-6 and a transgene constructs that directly reduce endogenous expression of chloride channels ClC-3, ClC-4, ClC-5, ClC-7, wherein the cell exhibits higher levels of ClC-6 and reduced levels of ClC-3, ClC-4, ClC-5, and ClC-7,

k) method of screening for compounds, using the claimed in vitro cells, does not reasonably provide enablement for

a) any natural in vitro cells that exhibit:

1. higher levels of ClC-7 expression than that of ClC-3 or ClC-6,

2. higher levels of ClC-7 expression than that of ClC-3, ClC-4, ClC-5, and ClC-6,

3. higher levels of ClC-7 expression than that of ClC-1, ClC-2, ClC-Ka, ClC-Kb, ClC-3, ClC-4, ClC-5, and ClC-6,

4. higher levels of ClC-3 and reduced levels of ClC-7,

5. higher levels of ClC-4 and reduced levels of ClC-7

6. higher levels of ClC-4 and reduced levels ClC-3, ClC-5, ClC-6, and ClC-7,

7. higher levels of ClC-6 and reduced levels of ClC-7

8. higher levels of ClC-3 and ClC-6 and reduced levels of ClC-7

9. higher levels of CIC-1, CIC-2, CIC-Ka, CIC-Kb, CIC-3, CIC-4, CIC-5, and CIC-6 and reduced levels of CIC-7

10. higher levels of CIC-6 and reduced levels of CIC-3, CIC-4, CIC-5, and CIC-7,

b) methods of screening for compounds, using non-genetically modified in vitro cells.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

While the art provides guidance for an artisan to arrive at in vitro cells that comprise a transgene construct that overexpresses a gene of interest and at in vitro cells that comprise a transgene construct that reduces expresses of a gene (e.g. a construct used in homologous recombination to disrupt a gene or a construct that expresses antisense), the neither the art nor the specification provides any guidance to arrive at any non-genetically modified cells from any animal, wherein the cell express or do not express specifically named chloride channels. The specification contemplates disruption of an endogenous gene (specification, page 5, lines 19- 30) or the use of antisense (specification, page 6, line 17), and the art teaches that overexpression constructs are commonly used to express a gene of interest. However, there is no guidance for an artisan to use the teachings of the art and specification to arrive at non-genetically modified cells, as encompassed by the claims.

As such, the claims are rejected.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 42-67 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant's arguments filed October 5, 2006 have been fully considered but they are not persuasive.

With regard to use of the phrase, "functionally expressed," Applicant indicates that a channel is functionally expressed if it is a) expressed and b) the form in which it is expressed is such that it is functional (Applicant's response, page 22, 1st parag.). In response, this is not persuasive because as indicated in the Office Action, it is unclear whether "preferentially functionally expressed" refers to a transgene construct or an endogenous gene that overexpresses ClC-7 (e.g. claim 42) as compared to ClC-3 and/or ClC-6. The phrase is also unclear because it can be interpreted that the cell, while it is preferred that the cell expresses wild type ClC-7 could alternatively comprise a transgene construct that expresses a dominant negative ClC-7. Because it is unclear whether the phrase, "preferentially functionally expressed" refers to a) a transgene construct, b) an endogenous gene, c) wild type ClC-7, or d) dominant negative ClC-7, the claims are ambiguous. It is noted that while the claims, as written, could be interpreted that the cells express dominant negative ClC-7, the specification provides no guidance that this was envisioned in the invention.

Applicant indicates that the phrase, "functionally expressed," is used frequently and is clearly understood in the art. Applicant indicates that US Patent 6,008,437 and 6,562,588 use the term "functionally expressed." In response, in the case of 6,008,437, the patent (e.g. claim 11) uses the term to indicate that the cell has no anthocyanin biosynthesis. There is no ambiguity to whether the claim was referring to a promoter that drove expression of the endogenous gene or to activity of a protein in the biochemical pathway because anthocyanin biosynthesis has to be terminated in order for the claim to be true. Similarly, in the case of 6,562,588, the abstract indicates that the invention is drawn to a CHO cell that does not express sialidase. Again, there is no ambiguity because the abstract indicates that the cell has no sialidase, regardless of whether one may be referring to a gene or a protein.

Applicant indicates that it is clear on the face of the word that if a first name channel is preferentially expressed with respect to a second named channel, there is to be a greater expression of the first than of the second. In response, this is not persuasive because claim 42 could be interpreted either as a) CIC-7 is overexpressed over CIC-3 and/or CIC-6, b) when CIC-3 and/or CIC-6 are expressed in a cell, it is preferred, but not required that CIC-7 is expressed in the cell, or c) it is preferred, but not required, that CIC-7, when it is expressed, it is functional, and that decision is made when CIC-3 and or CIC-6 are present in the cell. While Applicant indicates an intended meaning in Applicant's response, page 22, parag. 4 to page 23, parag. 1, the claims, as written, have multiple meanings that it is unclear what the metes and bound of the claims are.

With regard to the phrase, "reduced functional extent," Applicant indicates that the term is clear on its face. Applicant indicates that if the channel is expressed to a reduced functional extent, one finds that the activity of the channel is reduced either because it is expressed to a reduced extent or because its functionality has been reduced, or both. In response, to clarify the issue, it is unclear what "functional extent" is relative to. For example, in claim 43, the claims can be interpreted as a) the expression levels of ClC-3 and ClC-6 are less than that of ClC-7, b) the expression levels ClC-3 and ClC-6 levels are reduced following an experimental manipulation, and c) the expression levels of ClC-3 and ClC-6 are less than that of another population of cells. It is unclear what the intended meaning of the claim is.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 42, 43 are newly rejected under 35 U.S.C. 102(b) as being anticipated by Grant and Acosta, 1996, Fundamental and Applied Toxicology, 33: 71-82, as evidenced by Davies et al., 2004, Molecular Vision, 10: 1028-1037.

Grant and Acosta teach cultured rabbit corneal epithelial cells (Grant et al., page 73, 1st col., under "Cell culture procedure").

While Grant and Acosta do not specifically teach that ClC-7 is expressed at higher levels than ClC-3 or ClC-6, Davies et al. teach that cultured rabbit corneal epithelial cells express ClC-7 at higher levels than that of ClC-6 (see Davies et al., page 1030, Figure 1A).

Thus, Grant and Acosta anticipate claims 42 and 43.

Claims 42-44 are newly rejected under 35 U.S.C. 102(b) as being anticipated by Johnson-Muller and Gross, 1987, PNAS, USA, 75: 4417-4421, as evidenced by Davies et al., 2004, Molecular Vision, 10: 1028-1037.

Johnson-Muller and Gross teach that rabbit corneal stromal cells were cultured (Johnson-Muller and Gross, page 4417 under Materials and Methods).

While Johnson-Muller and Gross do not specifically teach that ClC-7 is expressed at higher levels than ClC-3 and ClC-6, Davies et al. teach that cultured rabbit corneal stromal cells express ClC-7 and that they express less ClC-3 than the epithelial cells and less ClC-6 than that of endothelial cells. Note that the claims only indicate that the cell needs to exhibit a reduction in expression; however, there is no indication as to what the expression is relative.

Thus, Johnson-Muller and Gross anticipate claims 42-43.

Claims 48, 49 are newly rejected under 35 U.S.C. 102(b) as being anticipated by Tamm et al., 1999, Invest. Opthalmol. Vis. Sci. 40: 2577-2582, as evidenced by Comes et al., 2005, Experimental Eye Research, 80: 801-813.

Tamm et al. teach cultured human trabecular meshwork cells (Tamm et al., page 2578).

While Tamm et al. do not specifically teach that CIC-3 is expressed at higher levels than CIC-7, Comes et al. do (Comes et al., page 806, Figure 1C).

Thus, Tamm et al. anticipate claims 48 and 49.

Claim 42-46 are newly rejected under 35 U.S.C. 102(b) as being anticipated by anticipated by Gupta et al., 1996, The Journal of Immunology, 157: 2123-2128 as evidenced by Kulka et al., 2002, Inflammation Research, 51: 451-456.

Gupta et al. teach cultured mast cells (Gupta et al, page 2123, under "Mast Cell Source").

While Gupta et al. do not specifically teach that CIC-7 is expressed, but chloride channels CIC-3, CIC-4, CIC-5, and CIC-6 are not expressed, Kulka et al. do (Kulka et al., page 454, Figure B2).

Thus, Gupta et al. anticipate claims 42-46

Claims 42-44, 50-53 are newly rejected under 35 U.S.C. 102(b) as being anticipated by Lee et al., 1998, Am. J. Physiol., 274: L450-L453, as evidenced by Mummery et al., 2005, Can. J. Physiol. Pharmacol., 83: 1123-1128.

Lee et al. teach cultured Calu-3 cells (Lee et al., page L450, 2nd col. under "Methods" to page L451, 1st col., 1st parag.). Mummery et al. teach that Calu-3 cells express CIC-7 more than CIC-3 and CIC-6 and that CIC-4 is expressed

more than ClC-3, ClC-5, ClC-6, and ClC-7 (Mummery et al., page 1126, Figure 2).

Thus, Lee et al., anticipate claims 42-44, 50-53.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Monday through Thursday and alternate Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the

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